201-15434A

IUCLID

Data Set

Existing Chemical	:	ID: 61788-32-7
CAS No.	:	61788-32-7
EINECS Name	:	Terphenyl, hydrogenated
EC No.	:	262-967-7
TSCA Name	:	Terphenyl, hydrogenated

Producer related part

Company	:	Solutia
Creation date	:	04.06.2004

Substance related part

Company	:	Revised by:Toxicology and Regulatory Affairs Freeburg IL rauckman@toxicsolutions.com
Creation date	:	04.06.2004
Status	:	
Memo	:	Hydrog Terphenyl
Printing date	:	13.06.2004
Revision date	:	
Date of last update	:	13.06.2004
Number of pages	:	30
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Solutia Inc.
Contact person	:	
Date	:	
Street	:	P.O. Box 66760
Town	:	Saint Louis, MO 63166-6760
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

04.06.2004

2.1 MELTING POINT

Value : -32 °C

Result :
As this material is a liquid at room temperature, the mp has been expressed as the pour point.

Test substance :
Partially Hydrogenated Terphenyl. mixed isomers, CASNO 61788-32-7

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.06.2004 (1)

2.2 BOILING POINT

Value : 359 °C at

Test substance :
Partially Hydrogenated Terphenyl. mixed isomers, CASNO 61788-32-7

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.06.2004 (1)

2.4 VAPOUR PRESSURE

Value : .002666 hPa at 25 °C
Decomposition :
Method :
Year :
GLP : no data
Test substance :

Method :
Gas saturation technique.

Remark :
Reported as 0.002 @ mm Hg 25 deg C.

Test substance :
MXP-2020, a precommercial sample of THERMINOL 66 of similar composition

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
04.06.2004 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 6.13 at 23 °C
pH value	:	
Method	:	Partition coefficient was determined via a direct partition experiment. At least two concentrations of the test substance were prepared in 100 ml of n-octanol. The n-octanol test solutions were combined with 500 ml purified water in a 1-l glass bottle at room temperature (ca. 25 deg. C) and shaken for 48 hours. Shaken mixtures were allowed to separate for 1 week in the dark. Concentrations of the test substance in each phase were determined by gas chromatography with dual flame-ionization detectors (GC-FID/FID). The partition coefficient (P) was calculated using the following equation: P = Co/Cw where Co and Cw are the concentrations of the test substance in n-octanol and water, respectively.
Result	:	Reported as 1.36x10E6.
Test substance	:	Santosol 340
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

04.06.2004 (3)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	< .06 mg/l at 23 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	OECD Guide-line 105
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Value cited was maximum value, as the methodology would not allow detection at lower levels.
Test substance	:	Santotherm 66
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

04.06.2004 (4)

3.1.1 PHOTODEGRADATION

Type	:	water
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 86 day(s)
Degradation	:	% after
Quantum yield	:	
Deg. product	:	
Method	:	other (measured)
Year	:	1982
GLP	:	no data
Test substance	:	

Method :

Direct analysis of photodegradation in sunlight. A 50 mg/L aqueous concentration using acetonitrile solvent was added to duplicate quartz tubes, sealed and exposed to sunlight (> 100 hrs over 15 day test period) at ave. temp. of 62 deg. F. Test sample was measured at intervals of 0, 2, 5, 9 and 15 days after exposure. Darkened tubes were also analyzed and amount of degradation subtracted from light-exposed tubes to define the degree of photolysis. Analysis conducted using GC-FID.

Result :

T 1/2 = 86 days

Test substance :

MXP-2020, a precommercial sample of THERMINOL 66 of similar composition.

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

13.06.2004 (5)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	= .000000000031 cm³/(molecule*sec)
Degradation	:	= 50 % after 4.1 hour(s)

Method :

AOP v1.90 (EPIWIN) calculation

Result :

AOP Program (v1.90) Results:==========
SMILES : C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1
CHEM : Dicyclohexyl benzene
MOL FOR: C18 H26 MOL WT : 242.41
---------- SUMMARY (AOP v1.90): HYDROXYL RADICALS ----------
Hydrogen Abstraction = 20.0005 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec**
Addition to Aromatic Rings = 10.9749 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec
OVERALL OH Rate Constant = 30.9754 E-12 cm3/molecule-sec
HALF-LIFE = 0.345 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 4.144 Hrs.....

..... ** Designates Estimation(s) Using ASSUMED Value(s)----------
SUMMARY (AOP v1.90): OZONE REACTION ----------
****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches

Test substance :

A representative structure of 1,3-Dicyclohexyl benzene (a major component of Partially Hydrogenated Terphenyls) with a SMILES notation of C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1.

Reliability : (2) valid with restrictions

Calculated by an acceptable method.

Flag : Critical study for SIDS endpoint

13.06.2004 (6)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	> 1 year at 25 °C
t1/2 pH7	:	> 1 year at 25 °C
t1/2 pH9	:	> 1 year at 25 °C
Deg. product	:	
Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	

Method :

Estimation on chemical principles

Result :

Stability in the aqueous environment, absent the presence of light, reactive chemicals, biological activity or redox activity, is determined by spontaneous decomposition and hydrolysis. Spontaneous decomposition is an inherent property of a molecule, while hydrolysis represents a reaction of the molecule of interest with water, typically producing products containing the elements of water. The occurrence and rate of a hydrolysis reaction is dependent on a large number of factors. The most important being if the reaction is energetically favorable; that is, do the reactants have less free energy than the products. Even if the reactants have overall lower free energy, the free energy of the transition state to get to these products may not be achievable under environmental conditions (March's

Advanced Organic Chemistry, fifth ed 2001).

Free energy is a combination of enthalpy and entropy and these are related by the well-known equation:

Delta-G = delta-H - T delta-S

A negative delta-G indicates a favorable reaction. Unless there is a change of state (e.g. liquid to gas) the entropy term for most reactions is small as compared to the enthalpy term. The enthalpy of reaction can be closely estimated by adding bond energies, resonance energies, bond strain and solvation energies and roughly estimated from bond energies and resonance energies.

Hydrolysis of aliphatic methylene group
Delta H =
400 kJ/mol (Aliphatic hydrogen-carbon bond)
497 kJ/mol (Hydrogen-hydroxy bond)
- 380 kJ/mol (Aliphatic hydroxy-carbon bond)
- 436 kJ/mol (Hydrogen-hydrogen bond)
Total = + 81 kJ/mol

Hydrolysis of aromatic hydrogen to phenol
Delta H =
473 kJ/mol (Aromatic hydrogen-carbon bond)
497 kJ/mol (Hydrogen-hydroxy bond)
- 472 kJ/mol (Phenolic bond)
- 436 kJ/mol (Hydrogen-hydrogen bond)
Total = + 62 kJ/mol

Both hydrolytic reactions have highly unfavorable delta-H (enthalpy of reaction) values and are therefore expected to take place only with the input of a large amount of energy. It is concluded that hydrolysis of this molecule will not occur under nominal environmental conditions.

Confirmatory information comes from Harris (Harris, JC. Rate of Hydrolysis in Handbook of Chemical Property Estimation Methods, Lyman and Reehl eds, ACS 1990) who notes that both alkanes and benzenes/biphenyls are functional groups that are generally resistant to hydrolysis.

Bond energies from Lide, Handbook of Chemistry 84th edition 2003-2004 section 9

Test substance :

Partially Hydrogenated Terphenyl. mixed isomers, CASNO 61788-32-7

Conclusion :

Estimated hydrolysis half-life is greater than 1 year.

Reliability : (2) valid with restrictions

Estimate by a reliable method

Flag : Critical study for SIDS endpoint

12.06.2004 (7) (8)

3.3.2 DISTRIBUTION

Media : other: water, soil, air, sediment
Method : Calculation according Mackay, Level III
Year : 2003

Method :

Level III fugacity based model, EPISUITE 3.10. Default values were assumed for environmental compartment descriptions, dimensions and properties, advective and dispersive properties. Chemical-specific modeling parameters as calculated by the model were: molecular weight= 242.41 g/mol, vapor pressure = 0.00012 hPa at 25 deg. C, log Kow = 7.63, melting point = 77.77 deg. C. and a Henry's Law constant of 0.00292 atm-m3/mol. Half-lives calculated by the model based on the properties of the test substance were: air half-life = 8.29 hr, water and soil half-lives = 900 hr, and sediment half-life = 3600 hr. Half-lives were considered reasonable based on limited experimental data. Emissions were assumed to be equal to air, water, and soil.

Remark :

This material is a complex mixture of partially hydrogenated polyphenols. 1,3-Dicychohexylbenzene is the major component and was selected as the representative structure to model. As physico-chemical properties for pure 1,3-dicychohexylbenzene have not been measured or found in the open literature, EPIWIN derived parameters were used in this calculation after examination for reasonableness. Other components are expected to show similar distributions as they have similar physico-chemical properties.

Result :

Media	Concentration
Air	0.229%
Water	3.57%
Soil	27.5%
Sediment	68.7%

Test substance :

A representative structure of 1,3-Dicyclohexyl benzene (a major component of Partially Hydrogenated Terphenyls) with a SMILES notation of C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1.

Reliability : (2) valid with restrictions

Calculation by recommended method.

Flag : Critical study for SIDS endpoint
12.06.2004 (9)

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: municipal sewage treatment plant
Concentration : 10 g/l related to Test substance
related to
Contact time : 9 month
Degradation : 35 - 1 (±8.6) % after 24 hour(s)
Result :
Deg. product :
Method : other: Semi-Continuous Activated Sludge (SCAS)
Year :
GLP : no

Test substance :

Method :

Nine-month SCAS test generally consistent with OECD guideline 302, 4 test periods of 4 to 29 days, 24-h cycle of draw and fill, weekly analyses of parent material using UV absorbance, while metabolites were quantified using GC-FID, 10 mg test material was added per cycle, activated sludge mixed liquor from municipal sewage treatment plant was inocula, a series of 3 hexane off-gas scrubbers were used to catch volatiles.

Result :

For time period 1, mean and 95% CI disappearance rate was 19.5 +/- 20.8%, for period 2 it was 55.0 +/- 12.9%, for period 3 it was 25.0 +/- 81.2% and for period 4 it was 48.6 +/- 6.9%. Overall mean daily disappearance rate was 35.1 +/- 8.6%. GC analyses showed that the several peaks that make up the test material degraded at varying levels. No volatile losses were reported.

Test substance :

HB-40

Conclusion :

The material displayed biodegradation sufficient to conclude that it would not be persistent in the environment.

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
11.06.2004 (10)

Type : aerobic
Inoculum : other: Meramec River water
Contact time :
Degradation : 68 (±) % after 50 day(s)
Result :
Deg. product :
Method : other: River-Die Away test
Year :
GLP : no
Test substance :

Method :

River water was obtained from the Meramec River near St. Louis, Missouri, USA. Settled water (2 days) was added (200 mL) to 16-oz. wide-mouth bottles. Distilled water controls (with test substance) were prepared similarly to assess sorption to glass and volatilization. Test material was added in 5 microliter volumes prepared with 4% (W/V) ethanol. Bottles were sealed with foil-lined caps and stored at room temperature in the dark for up to 50 days. A positive control (LAS Reference #2 - Dodecene-1) was prepared similarly and used to verify the biological activity. Periodically, chemical analyses were made by sacrificing a bottle containing test material and a control.

Three 50-mL aliquots of hexane were injected into the bottle, the bottle vigorously shaken, and the phases allowed to separate. The three portions of hexane were collected, concentrated to 10 mL using a Kudema-Danish concentrater, transferred to a 10 mL cell and the UV absorption determined. Recoveries of spiked samples for the test substance were 91.6%.

Result :

Losses from the distilled water control were 13%. Test material was reduced by 68% in 21 days and by 81% (net loss of 68%) in 50 days.

Test substance :

HB-40

Conclusion :

The material displayed biodegradation sufficient to conclude that it would not be persistent in the environment.

Reliability : (2) valid with restrictions

Supplemental information which indicates biological breakdown in the environment.

11.06.2004 (10)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> .06
Limit test	:	yes
Analytical monitoring	:	no
Method	:	other: US EPA 660/3-75-009
Year	:	
GLP	:	yes
Test substance	:	

Method :

This study followed US EPA guideline 660/3-75-009. 1975. Committee on Methods for Toxicity Tests with Aquatic Organisms. Fathead minnows were obtained from a fish hatchery, held in culture tanks for two weeks under 16 hrs light, 8 hrs dark. Fish were fed commercial fish food until 48 hr before the test. Fish had a mean weight and length of 0.46 g and 30.4 mm, respectively. Static bioassay was performed in a 40 L glass aquaria containing 30 L of laboratory well water and 10 (ten) fish per concentration. Antimycin a was used as a positive control. Water quality of test dilution at test initiation was: DO 9.3 mg/L, pH 7.8-8.2, total hardness of 255 mg/L CaCO3, total alkalinity of 368 mg/L CaCO3. Test water was maintained at 22 +/- 1 deg. C in a water bath. Fish were held without food for 48 hrs before testing and were not fed during the test. Based on finding no toxicity at 1000 mg/L in a range-find test, a definitive test was conducted at 1,000 mg/L nominal test material. A test concentration was prepared by adding test material directly to the test vessel; no meaurements of test material were taken during the test. An oily film was observed in the test vessels during the study. Across all test vessels, DO varied between 5.2 to 8.5 mg/L, pH ranged from 7.3-8.3, temperature remained close to 22 deg. C.

Result :

No control mortalities were observed and only 10% deaths were seen in the 1000 mg/L Limit Test dose after 96 hours of testing. Thus the 96-h LC50 was > 1000 mg/L nominal. As the water solubility of the test agent is less than 0.06 mg/L., then the LC50 correctly stated is > 0.06 mg/L.

Test substance :

Therminol 66

Reliability : (2) valid with restrictions

While the nominal dose level used in this study well exceeded the water solubility of Therminol 66, it can reasonably be concluded that the 96-h EC50 is in excess of the water solubility limit, as the nominal concentration proved to produce only limited (10% deaths) toxicity.

Flag : Critical study for SIDS endpoint

13.06.2004 (11)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	> .06
Limit test	:	yes
Analytical monitoring	:	no
Method	:	other: US EPA 660/3-75-009
Year	:	
GLP	:	yes
Test substance	:	

Method :

This study followed US EPA guideline 660/3-75-009. 1975. Committee on Methods for Toxicity Tests with Aquatic Organisms. Rainbow trout were obtained from a fish hatchery, held in culture tanks for two weeks under 16 hrs light, 8 hrs dark. Fish were fed commercial fish food until 48 hr before the test. Fish had a mean weight and length of 1.02 g and 39.1 mm, respectively. Static bioassay was performed in a 5 gal. glass aquaria containing 15 L of laboratory well water. Ten (10) fish per test concentration level were used. Antimycin A was tested as a positive control. Water quality of test dilution at test initiation was: DO 8.9 mg/L, pH 7.8, total hardness of 240 mg/L CaCO3, total alkalinity of 360 mg/L CaCO3. Test water was maintained at 12 +/- 1 deg. C in a water bath. Fish were held without food for 48 hrs before testing and were not fed during the test. Based on finding no toxicity at 1000 mg/L in a range-find test, a definitive test was conducted at 1,000 mg/L nominal test material. A test concentration was prepared by adding test material directly to the test vessel; no meaurements of test material were taken during the test. An oily film was observed in the test vessels during the study. Across all test vessels, DO varied between 5.8 to 7.3 mg/L, pH ranged from 7.3-8.3, temperature remained at 12 deg. C.

Test Substance : Therminol 66

Reliability : (2) valid with restrictions

Provided as Supplemental information. While the nominal dose level used in this study well exceeded the water solubility of Therminol 66, it is reasonable conclude that the 96-h EC50 is in excess of the water solubility limit (0.06 mg/L), as the nominal concentration proved to produce only limited (10% deaths) toxicity.

13.06.2004 (12)

Type	:	other
Species	:	other: calculated
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= .00092 calculated

Method	:	other: calculation based on ECOSAR
Year	:	2003
GLP	:	no
Test substance	:	
Method	:	96-Hr Fish LC50 calculation using ECOSAR, from the USEPA. Value was calculated using a calculated log Kow of 7.63. The SAR for neutral organics was employed.
Remark	:	Provided as Supplemental Information to this HPV data package.
Test substance	:	A representative structure of 1,3-Dicyclohexyl benzene (a major component of Partially Hydrogenated Terphenyls) with a SMILES notation of C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1.

13.06.2004 (13)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= 1.34
EC50	:	> 1.34
Limit Test	:	yes
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202
Year	:	
GLP	:	yes
Test substance	:	
Method	:	Twenty < 24-h old D. magna Straus were tested at 20 +/- 1 deg. C in a series of four replicates per test concentration. The Limit Test was conducted at 1.34 mg/L and included clean water and solvent (ethoxylated triglyceride at 150 mg/L) controls. Stock solutions had a few white dust-looking particles floating on their surface. Tests were conducted using reconstituted distilled water. Water was reconstituted with CaCl2, MgSO4, NaHCO3 and KCl. At test initiation, the pH was 7.97. DO was at 23.8% of saturation, specific conductance was at 680 micro-siemens, hardness was 262 mg/L, alkalinity was 34 mg/L. Test concentrations were measured using HPLC. Daphnids were not fed during the test. Tests were conducted in 1 fluid ounce plastic cups containing 25 mL of solution. Dissolved oxygen, temperature and pH were monitored at the beginning and end of the test. At test initiation, the test substance concentration was 1.34 mg/L and at 28 hr it was 1.29 mg/L. A photoperiod was not specified in the report. However, as this study was conducted in late July/early August in St. Louis Mo. the average photoperiod in that location is approximately 16-h light,8-h dark.

Result	:	Limit Test 48-h EC50 = >1.34 mg/L; 24-h EC50 >1.34 mg/L. NOEC = 1.34 mg/L. There were no immobilizations reported in either control or in vessels with test substance at either 24 or 48 hrs. At test initiation, pH ranged from 7.96 to 8.03, DO ranged from 17.3 to 23.4% of saturation and temperature ranged from 22 to 23 deg. C. At 48 hrs, pH ranged from 7.77 to 8.02, DO ranged from 20.1 to 22.7% of saturation, and temperature ranged from 20.4 to 21.6 deg. C.
Test substance	:	THERMINOL 66
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

13.06.2004 (14)

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
NOEC	:	= .056
EC50	:	= .1
Method	:	other
Year	:	
GLP	:	yes
Test substance	:	
Method	:	Followed guidance according to EPA 660/3-75-009. Ten < 24-h old D. magna Straus were tested at 20 +/- deg. C. in a series of two replicates per test concentration. Test concentrations were 0.056 (level of solubility), 0.10, 0.18, 0.32 and 0.56 mg/L, plus clean water and solvent (acetone) controls. Tests were conducted using well water from Columbia, MO. Concentrations were not measured. Daphnids were not fed. Tests were conducted in 250-mL beakers containing 200 mL of solution. Dissolved oxygen was monitored to ensure the concentration did not fall below 2 mg/L before the end of the test. Water quality was measured for dissolved oxygen, pH, ammonia, and temperature and no significant changes were observed in any parameter during the test. The estimated EC50 and 95% confidence limits were determined using EPA statistical procedures (probit analysis).
Remark	:	Supplemental information
Result	:	48-h EC50 (95% CL) = 0.10 (0.075-0.13) mg/L; 24-h EC50 (95% CL) = 0.70 (0.49-1.0); NOEC = < 0.056 mg/L.; At 24-h, there were no mortalities in controls or the lower two test concentrations. Clumping of daphnids was observed at the highest 3 concentrations. At 48-h, there were no mortalities (0/10; 0/10) in controls. There were partial mortalities in the lower three test concentrations [2/10;2/10 @ 0.056 mg/L; 4/10,5/10 @ 0.10 mg/L;8/10, 10/10 @0.18 mg/L]and 100% mortality in the highest two (0.32 &

0.56 mg/L) concentrations. Mortalities followed a dose-response pattern.

Test substance :

Therminol 66

Reliability : (2) valid with restrictions
13.06.2004 (15)

Type : other: Calculation
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = .00145 calculated
Method : other: calculation using ECOSAR
Year : 2003
GLP : no
Test substance : other TS

Method :

48-Hr Daphnia LC50 calculation using ECOSAR, from the USEPA. Value was calculated using a calculated log Kow of 7.63. The SAR for neutral organics was employed.

Remark :

Provided as Supplemental Information to this HPV data package.

Test substance :

A representative structure of 1,3-Dicyclohexyl benzene (a major component of Partially Hydrogenated Terphenyls) with a SMILES notation of C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1.

13.06.2004 (13)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : other: chlorophyl a, cell number
Exposure period : 96 hour(s)
Unit : mg/l
EC50 (chlorophyl a) : > .06
EC50 (cell number) : > .06
Limit test :
Analytical monitoring : no
Method : other: US EPA, 1971.
Year :
GLP : no data
Test substance :

Method :

The study followed methods outlined in USEPA, 1971. Algal Assay Procedure: Bottle Test. National Eutrophication Research Program. Pacific Northwest Water Laboratory, Corvallis, OR. Cultures were incubated at 24 +/- deg. C under 4000 lux illumination during a 24-h/d photoperiod. Triplicate culture flasks were employed for each of the test concentrations and controls used. Nominal test concentrations were 10, 32, 56, 100 and 320 mg/L. Both clean water and solvent controls were included.

Dimethylformamide (DMF) was used as a cosolvent (0.05 mL per test flask). Test material was dissolved in DMG and directly added to the test vessels. Initial cell counts were ~ 20,000 cells/mL. Light intensity was approximatly 4000 lus chlorophyll a was measured using a Turner Model 111 fluorometer. Cell counts were made every 24 hours using a hemacytometer and a Zeiss Standard 14 compound microscope. Specifics of the culture medium were not provided other than stating that test medium was based on USEPA guidance. Results were analyzed using the Student's t test. PH was maintained between 7.2 and 7.4 during the test.

Result :

Chlorophyll a
96-h EC50 (95% CI) = 44 (1-1586) mg/L.
24-h EC50 (95% CI) = >320 mg/L
48-h EC50 (95% CI) = >320 mg/L
72-h EC50 (95% CI) = >100 < 320 mg/L.

Cell number
96-h EC50 (95% CI) = 56 (4-743) mg/L.

As the water solubility of THERMINOL 66 is less than 0.06 mg/L, this level was exceeded in both phases of this study. However, as there were no toxic effects observed at the lowest dose tested, it can be concluded that the EC50 > 0.06.

Test substance :

Therminol 66

Reliability : (2) valid with restrictions

All test levels exceeded the water solubility limit of Therminol 66 of less than 0.06 mg/L. However, the lowest dose levels in this study did not produce a treatment-related effect. Thus, it can be concluded that no effects were seen up to the level of water solubility for this material.

Flag : Critical study for SIDS endpoint

13.06.2004 (16)

Species : other algae
Endpoint : other: calculation for green algae
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = .00125 calculated
Method : other: calculation based on ECOSAR
Year : 2003
GLP : no
Test substance :

Method :

96-Hr Algae EC50 calculation using ECOSAR, from the USEPA. Value was calculated using a calculated log Kow of 7.63. The SAR for neutral organics was employed.

Remark :

Provided as Supplemental Information to this HPV Package.

Test substance :

A representative structure of 1,3-Dicyclohexyl benzene (a major component of Partially Hydrogenated Terphenyls) with a

SMILES notation of C(CCCC3)(C3)c(cccc1(C(CCCC2)C2))c1.

13.06.2004 (13)

5.1.1 ACUTE ORAL TOXICITY

Type	:	other: Limit Test
Value	:	> 10000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: administered neat
Doses	:	10,000 mg/kg
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	
GLP	:	yes
Test substance	:	

Method :

A single group of 5 male and 5 female fasted SD rats were administered 10,000 mg/kg test material via gavage and observed for 15 days. Twice daily examinations were made for mortality and signs of toxicity. Body weights were recorded on the first day of testing and weekly thereafter. Food and water were given ad libitum. Temperature, humidity and light cycle were controled. At the end of the study, all survivors were given a full necropsy.

Result :

No deaths occurred at the single dosage level tested of 10,000 mg/kg. Signs of toxicity included: hypoactivity, diarrhea and feces- and urine- stained fur. All animals were normal at necropsy.

Test substance :

HB-40

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

12.06.2004 (17)

Type	:	other: Limit Test
Value	:	> 24000 mg/kg bw
Species	:	rat
Strain	:	Fischer 344
Sex	:	female
Number of animals	:	
Vehicle	:	other: undiluted
Doses	:	no data available
Method	:	other
Year	:	
GLP	:	no
Test substance	:	

Method :

Female F344 rats, 12-14 weeks old, were fasted overnight and then dosed by gavage with undiluted test material. No dosage exceeded 24 g/kg bw. Five rats per treatment group were tested using dosages spaced at 0.1 log increments. Animals were maintained at 20 +/- 2 deg. C, 12-hr light:dark cycle

and had water and food provided ad libitum. Daily observations for clinical signs were taken throughout the 14-day test period; body weights were recorded prestudy and weekly thereafter. Gross pathological examinations were carried out on selected animals which survived the highest dose tested. As this study resulted in a Limit Test, no LD50 calculation, using the method of Deichmann and LeBlanc, was made.

Result :

LD50 value was determined to be above the highest dose tested of 24,000 mg/kg. Other than diarrhea during the first 24-hrs, no other clinical signs of toxicity were reported. No evidence of gross pathological effects were reported.

Test substance :

Test material was referenced as commercial grade THERMINOL 66, obtained from Monsanto Co.

Reliability : (2) valid with restrictions

This information is supplied as Supplemental to a previously reported Limit Test by the oral route.

12.06.2004 (18)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	oral feed
Exposure period	:	91 days
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	50, 200, 2000 ppm
Control group	:	yes
NOAEL	:	= 200 ppm
LOAEL	:	= 2000 ppm
Method	:	OECD Guide-line 408 "Subchronic Oral Toxicity - Rodent: 90-day Study"
Year	:	
GLP	:	yes
Test substance	:	

Method : Groups of 12 male and 12 female SD rats (approx. 4 wks old) were administered a diet admixed directly with test material for 91 days. Levels of test material were verified during weekly diet analysis. All rats were examined for morbidity and mortality twice daily. Body weights and food consumption were measured weekly, and detailed signs of toxicity recorded. Humidity, temperature and lighting were controled. Clinical pathology for the following indices were measured for 10 rats/sex/group after 1 and again after 3 months on

test: Hematology - HCT, HGB, RBC, WBC, Platelets, erythrocyte morphology and differ. leukocytes; Serum Chemistry - Ca, In. Phos, CL, Na, K, GLU, ALT, AST, BUN, Albumin, globulin, T. Prot., Creat., T. Bili and GGTP. An ophthalmoscopic examination was given to all rats prior to study start and at study term. At the end of the study, all rats were given a necropsy and organ weights and body:organ weight ratios recorded for: brain, kidney, liver, testes and adrenals. Histopathological examination of a full set of tissues and organs, including ovaries, testes,adrenals, aorta, bone, marrow, femur, brain, esophagus, eyes, exorbital lacrimal gland, heart, intestines (6 sections), kidneys, liver, lungs, lymph nodes, mammary gland, uterus, pancreas, pituitary, prostate, salivary gland, seminal vesicles, skel. muscle, skin, spinal cord, nerve, spleen, stomach, thymus, thyroid/parathyroid, trachea, epididymides and all gross lesions were given to all rats in the control and high dose group. Livers, Lungs and kidneys from all mid and low dose animals were also examined microscopically. Statistical analysis of body weights, food consumption, growth rates, clinical pathology, organ weights and ratios were performed using Leven's Test for homogeneity and ANOVA followed by Terpstra-Jonckheere test and Dunnett's test for group-wise comparison.

Remark :

Based on food consumption and body weight data conversion factors, the dosages of test articles employed in this study were approximately 150, 15 and 3.5 mg/kg/d.

Result : The NOAEL for this study is considered to be 200 ppm.

The following treatment-related effects seen at 2000 ppm were minimal in nature: small decreases in body weight in males (2.7%) and females (6-7%). Small but statistically significant decreases in hemoglobin, hematocrit and erythrocyte count were observed in high dose males, but not females, at the 1 month interval, but were no longer statistically significant at study termination. A statistical increase in platelet counts was seen in this study group at both the 1 and 3 month interval. Cholesterol and albumin were elevated in high dose males after 3 months (cholesterol also after 1 mo.). Both males and females exhibited increased absolute kidney and liver weight increases as well as corresponding increased organ/body and organ/brain weight ratios. Microscopic evaluation resulted in no morphological evidence of a direct toxicopathologic effect of treatment. High dose males, but not females, had an increased incidence (but similar level of severity) of a spontaneously occurring regenerative renal lesion also present in control male rats. The pathological significance of this finding was deemed unclear. No treatment-related effects were seen on male or female reproductive organs.

Source :
Test substance : Therminol 66
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

12.06.2004 (19)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium tester strains TA 1535, 1537, 1538, 98 and 100
Test concentration	:	1 to 10,000 ug/plate
Cycotoxic concentr.	:	not reported; none apparently seen up to highest dose tested
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: Ames et al. 1975. Mutat. Res. 31:347-364.
Year	:	
GLP	:	no
Test substance	:	

Method :

Method of testing and evaluation used the procedures described in Ames et al, 1975, Mutat. Res. 31:347-354. Test samples diluted in dimethyl sulfoxide were prepared to give final concentrations ranging from 1 to 10,000 ug/plate in 0.1 ml. Negative and positive controls were used. Each of 5 Salmonella tester strains, TA1535, 1537, 1538, 98 and 100 were tested in replicate plates with and without inclusion of liver homogenates from Arochlor 1254-treated male rats as the activation system.

Positive controls were:
TA-1535 and TA-100: N-Methyl-N'-nitro-N-nitrosoguanidine 10 ug/plate

TA-1538, TA-98 and TA-100: 2-aminofluorene, 10 ug/plate

TA1537: 9-aminoacridine 50ug/plate

Statistical criteria for a positive result were not given. The only criteria mentioned in the article was that none of the test substances caused reproducible, dose-related mutagenic activity.

Result :

No significant mutagenic activity seen in any of the Salmonella tester strains used, with or without metabolic activation.

Test substance :

Test material was referenced as commercial grade THERMINOL 66, obtained from Monsanto Co.

Reliability : (2) valid with restrictions

No data shown in peer-reviewed publication; however, raw data is on file at the Environmental Mutagen Information Center, Oak Ridge, Tenn.

Flag : Critical study for SIDS endpoint

13.06.2004 (18)

Type	:	Ames test
System of testing	:	Salmonella tester strains TA 1535, 1537, 98, 100
Test concentration	:	10, 3, 1, 0.2, 0.04, 0.01 ul/plate
Cycotoxic concentr.	:	> 100 ul/plate
Metabolic activation	:	with and without

Result	:	negative
Method	:	OECD Guide-line 471
Year	:	
GLP	:	yes
Test substance	:	
Method	:	Method used was plate incorporation assay based on Ames test methods consistent with OECD 471. A single test was run in triplicate at each dosage both with and without metabolic activation. The S-9 liver homogenates were prepared from male rats and given Arochlor 1254. All tester strains were obtained from Dr. B. Ames. Sterile DMSO was used as the solvent and a solvent control was employed of 20 uL/plate DMSO. Positive controls used were: 2-aminoanthracene, NaNo2 and 2-nitrofluorene. A positive response was determined upon observation of a statistically significant dose-response increase in revertant colonies. Bartlett's test was used for pairwise comparison to controls and dose response determined using regression analysis for log-log straight lines; P<0.01 was used.A spot test was also conducted using a single dosage of 50 ul/plate with and without S-9. A toxicity test was run using TA-100 with and without S-9 at dosages of 100, 30, 10, 1, 0.3, and 0.1 ul/plate.
Result	:	No mutagenic changes were observed in any of the four tester strains used, with or without metabolic activation. No effects on background lawn were observed up to 100 ul/plate. No treatment-related mutagenic effects were observed in the Spot test, with or without metabolic activation, in any of the four tester strains.
Test substance	:	HB-40
Reliability	:	(2) valid with restrictions Study limited to 4 of 5 Salmonella tester strains called for in test guidelines and used only a single test without confirmation. Highest test dose was below limit of toxicity. However, study confirms results of previously reported Salmonella test used to fulfill this HPV endpoint.

12.06.2004 (20)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Cytogenetic assay
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	i.p.
Exposure period	:	24 hours
Doses	:	250, 1250, 2500 mg/kg
Result	:	negative
Method	:	OECD Guide-line 475 "Genetic Toxicology: In vivo Mammalian Bone Marrow Cytogenetic Test - Chromosomal Analysis"
Year	:	
GLP	:	yes

Test substance :

Method :

Dose levels selected based on both a range-find study followed by a pilot study where severe signs of toxicity and deaths (8/10) were seen at 5000 mg/kg test agent, the highest dose used in this study design. Six Fischer-344 rats/sex/time period were administered test agent in corn oil by intraperitoneal injection. Metaphase cells were collected from rat bone marrow (femur) at harvest times of 6, 12 and 24 hrs after treatment. Colchicine was administered 2 hr prior to sacrifice to arrest cells in c-metaphase. Marrow was exposed to hypotonic solution and fixed, cells and slides prepared and stained. All slides were coded before reading. Positive (Triethylene melamine) and negative (corn oil and untreated) controls were used for comparative purposes. Mitotic index was calculated based on counting of at least 1000 slides and chromosomal aberrations evaluated from at least 60 slides per animal per time point from the untreated control groups (male and female) and the 2,500 mg/kg test groups. All breaks, deletions, translocations and other changes were recorded. Mitotic Index, % chromosomally aberrant cells and frequency of chromosomal aberrations per cell were compared between treated vs control groups using ANOVA and Dunnett's test. P <0.05 was used.

Result :

No significant differences in % chromosomally aberrant cells or frequency of chromosomal aberrations/cell were observed between the negative control group and any of the test article treated groups at any of the three time points investigated. The positive control performed as expected. No evidence of cytotoxicity was observed at any test level.

Test substance :

Therminol 66

Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
12.06.2004 (21)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : Two generation study
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : F0 & F1 Adults-premating through litter weaning (Fo) and postweaning (F1)
Frequency of treatm. : daily
Premating exposure period
Male : FO- 14 weeks; F1- 18 weeks
Female : FO- 14 weeks; F1- 18 weeks
Duration of test : FO M/F - 167d; F1 M/F- 219d

No. of generation studies	:	2
Doses	:	30, 100, 300, 1000 ppm
Control group	:	yes, concurrent vehicle
NOAEL parental	:	= 1000 ppm
NOAEL F1 offspring	:	= 1000 ppm
NOAEL F2 offspring	:	= 1000 ppm
Method	:	OECD Guide-line 416 "Two-generation Reproduction Toxicity Study"
Year	:	
GLP	:	yes
Test substance	:	

Method :

Test material was administered in the diet to groups of 30M and 30F rats of the F0 and F1 generations during a premating (70 days) growth period, and through the ensuing mating, gestation and lactation intervals (1 litter/generation) until day 21 post-partum. Dietary concentrations were analyzed by GC-FID weekly (all test levels first 4 weeks of the study, then one dose level weekly thereafter) to establish stability, homogeneity of mixing and target concentration accuracy. Body weights were recorded weekly for F0 and F1M. For F0 and F1 F wts were recorded weekly through the growth period and up to mating, then resumed after mating until sacrifice. Food consumption was recorded weekly for F0 and F1 M from study start up to mating, then resumed after mating through study term. Food consumption for adult females F0 and F1 was recorded weekly through the growth period and again after weaning of litters. Cageside observations for morbidity and mortality were made weekly, as well as daily observations of clinical signs.
Temperature, humidity and light-dark cycles were controlled.
F0 and F1 adults were sacrificed following weaning of their respective litters and given a gross postmortem examination. Reproductive tissues (testes, epididymides,seminal vesicles,uterus,vagina, mammary glands, prostate, ovaries) and selected other tissues (liver, pituitary, skin, and all gross lesions) were evaluated histopathologically for all control and high dose animals. Pups delivered to F0 and F1 females were evaluated for growth, survival and external irregularities during lactation days 0, 4, 7, 14 and 21. F1 pups not selected for the adult generation were sacrificed and given a gross postmortem exam. Body weights and changes, food consumption, gestation length and number of offspring were analyzed using ANOVA techniques followed by Dunnet's Test for parametric parameters and Kruskal-Willis test, Jonckheere or Mann-Whitney methods for nonparametric analysis. Mortality and pregnancy rates, fetal and mating indices and pup survival were analyzed using uncorrected Chi-square. Fisher's Exact test was used to statistically evaluate microscopic lesions. The level of significance was reported at both the 5% and 1% levels.

Result :

No Adverse reproductive effects were observed in adult rats or their offspring up to the highest dose tested, i.e. 1000 ppm, the reproductive NOAEL for this study.

Small, statistically significant decreases in body weights were observed in High Dose (1000 ppm) F0 males during the last three weeks on test (mean wts 94% of control) and in F1a dams of the same dose group (mean weights 93% of control) during lactation days 0-7. Food consumption was statistically reduced in 1000 ppm F0 females during the first 2 weeks of gestation. These minor deviations from the norm are not considered sufficiently severe to constitute an adverse effect. Thus, the NOAEL for non-reproductive toxicity is considered 1000 ppm.

No treatment-related effects were noted in mating or fertility indices nor were any microscopic lesions attributable to treatment observed in reproductive organs (and other tissues) examined microscopically.

Daily average group mean dosages were calculated based on raw data for food consumption and body weight and were as follows:
Group (PPM): 30 100 300 1000

F0 males - 1.8, 6.1, 18.5 62.0 mg/kg/day
F0 females - 2.5, 8.3, 42.2, 81.2 mg/kg/day

F1 males - 1.9, 6.1, 18.2, 63.1 mg/kg/day
F1 females- 2.4, 8.1, 24.3, 80.6 mg/kg/day

Test substance :

Terminol 66

Reliability : (2) valid with restrictions

Hematology, clinical chemistry, FOB and organ weights not conducted in this study, although all parameters were measured in subchronic study cited in this data package. Study itself sufficient to adequately judge fertility and reproductive indices.

Flag : Critical study for SIDS endpoint

12.06.2004 (22)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Crj: CD(SD)
Route of admin.	:	gavage
Exposure period	:	Day 6-15 of gestation
Frequency of treatm.	:	Once daily
Duration of test	:	
Doses	:	125, 500 or 1500 mg/kg-day
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	= 500 mg/kg bw
NOAEL teratogen.	:	= 500 mg/kg bw
LOAEL Maternal Toxicity	:	= 1500 mg/kg bw
other: LOAEL Developmental	:	= 1500 mg/kg bw
Result	:	Not a specific developmental toxin

Method : OECD Guide-line 414 "Teratogenicity"
Year : 1981
GLP : yes
Test substance :

Method :

Dose levels were selected based on a preliminary range-finding study.

The test substance was dissolved in corn oil (prepared fresh weekly) and administered by gastric intubation to mated CD rats (24 females/group) at dose levels of 0, 125, 500 and 1500 mg/kg-day during on days 6-15 of gestation. Representative dosing solutions were analyzed for test substance and homogeneity. During gestation, body weights were recorded for individual females on days 0, 6, 9, 12, 15 and 20 of gestation and food consumption was recorded for the day 0-6, 6-9, 9-12, 12-15 and 15-20 gestation intervals. Additionally, each female was given a detailed physical evaluation periodically throughout the study.

Surviving females were sacrificed on Day 20 of gestation, given a "complete" gross postmortem evaluation and corpora lutea/uterine implantation data recorded. Fetuses recovered at this time were weighed, sexed and given a gross external examination for malformations, Subsequently, one-half of the fetuses in each litter were processed for visceral evaluation (micro dissection procedure) and the remaining fetuses evaluated for skeletal malformations/ossification variations (Alizarin Red stained specimens),

STATISTICAL METHODS:
Data were analyzed by one of two methods.

The Interval Data Method (see below) was used for:
- Mean body weights - gestation
- Mean weight change - gestation
- Mean food consumption
- Mean number of corpora lutea
- Mean number of implantation sites
- Mean number of live fetuses
- Mean number of resorptions
- Pre-Implantation loss ratio (individual females)
- Resorption/implant ratio (individual females)

The Incidence Data Method was used for:
- Mortality Rates
- Pregnancy Rates
- Incidence of fetuses with malformations/variations
- incidence of litters containing fetuses with malformations/variations.
- Incidence of females with resorption sItes

INTERVAL DATA METHOD:
Statistical evaluation of equality of means was made by the appropriate one way analysis of variance technique, followed by a multiple comparison procedure if needed. First, Bartlett's test was performed to determine if groups had equal variance. If the variances mere equal, parametric procedures were used; If not, nonparametric procedures were used. The parametric procedures were the standard one way ANOVA using the F distribution to assess significance. If significant differences among the

means were indicated, Dunnett's test was used to determine which means were significantly different from the control. If a nonparametric procedure for testing equality of means was needed, the Kruskal-Wallis test was used, and if differences were indicated a summed rank test, (Dunn) was used to determine which treatments differed from control.

A statistical test for trend in the dose levels was also performed. In the parametric case (i.e., equal variance) standard regression techniques with a test for trend and lack of fit were used. In the nonparametric case, Jonckheere's test for monotonic trend was used.

The test for equal variance (Bartlett's) was conducted at the 1% two-sided risk level. All other statistical tests were conducted at the 5% and 1%, two-sided risk level. All ratios were transformed via the arc sine transformation prior to analysis.

Remark :

This result is supported by the results of a two-generation feeding study conducted in rats at feed levels of 0, 30, 100, 300 or 1000 ppm*. In this study, developmental parameters were not affected. Although administration of the high-dose was associated with minor reduction in group weight gains of the F0 males near the end of the study and a slight reduction in group weight gains of the F1a dams during gestation the high-dose of 1000 ppm is considered a reproductive and developmental NOAEL while the overall NOAEL for systemic effects is considered to be 300 ppm.

The amount of test substance that the females were exposed to based on the target concentrations of test substance in feed and average feed consumptions were 2.5, 8.3, 20.4 and 81.2 mg/kg-day. Even with increased feed consumption of the pregnant dams, it is doubtful that the test substance exposure reached the low dose level (125 mg/kg-day) of the definitive developmental toxicity study. Because of this, and the lack of effects the developmental data from the two-generation study are not presented in detail.

*Solutia Study no. ML-90-135. 1991. Two Generation Reproduction Study of THERMINOL 66 Heat Transfer Fluid in the Diet of Albino Rats.

Result :

No mortality occurred in the control. low- or mid-dose groups. At the high-dose level, a total of four females died; however, the death of one female was attributed to an intubation error. Excluding this one female, the mortality rate in the high-dose group was 12.5%.

No adverse effect of treatment was evident in pregnancy rate data. The pregnancy rate was 100% in the control, mid- and high dose groups and 91.7% (22/24) in the low-dose group.

Body Weights: At the low and mid-dose levels, mean body weight and mean weight gain data during the treatment or post-treatment periods were not considered adversely affected by treatment. Although mean weight gain was 14.8% lower in these groups than controls, this change was not statistically significant (and was mainly the result of two dams in each group that showed little weight gain in this period).

At the high-dose level, mean body weights were significantly lower than control on Days 9 (13.5%), 12 (11.2%), 15 (11.1%) and 20 (9.4%) of gestation and mean weight gain during the Day 6-15 gestation interval was

significantly lower (104 versus 131 g, 20.6%) than controls for this same group.

Food Consumption: No effect on food consumption was evident at the low-dose level. In the mid-dose group, mean food consumption was significantly lower than control during the Day 6-9 and 9-12 gestation intervals and in the high-dose group, mean food consumption was significantly lower than control only during the gay 6-9 gestation interval. A statistically significant increase in mean food consumption data for the high-dose group during the Day 15-20 gestation interval was not considered indicative of an adverse effect of treatment.

Physical Evaluations: At the low-dose level, no adverse effect of treatment was evident from the detailed physical evaluations. At the mid-dose level, the incidence of females with areas of alopecia was notably increased at Days 16 and 20 of gestation; no other adverse effects of treatment at the mid-dose level were evident from the physical In-life observation data. At the high-dose level, the incidence of females with staining of the fur in the ano-genital area and/or soft stool was increased during the treatment interval of gestation. Additionally, several high-dose females were noted early in gestation (Day 9) as emaciated with red material about the snout.

Implantation Data: No adverse effect of treatment at the low- or mid-dose level was evident from uterine implantation data. An increase in both the mean number of resorption sites (1.1 versus 0.4 per dam) and the mean ratio of resorptions to implants (0.091 versus 0.024) was seen at the high-dose level. These resorption data did not differ statistically from control data and the mean number of resorption sites at the high-dose level was well within the range of historical control data for this laboratory, Thus, it is not clear if the increase in resorption data seen at the high-dose level represents an adverse effect of treatment. The number of corpora lutea was reduced in the high dose dams (296 versus 378, 24 pregnant dams per group) as was the number of implantation sites (346 versus 378).

No adverse effect of treatment was evident in fetal weight data or fetal sex distribution data at the low- and mid-dose levels. In the high-dose group, mean fetal weight was significantly lower than control (high-dose 3.26 g, control 3.67 g mean); however, fetal sex distribution data were not adversely affected.

Malformations: No increase in the incidence of malformations was seen during the external, visceral or skeletal evaluations of fetuses recovered from females treated at the low- or mid-dose levels.

Air the high-dose level, no increase in malformation rate was seen during fetal external evaluations; however, the incidence of fetuses with a glassy (shiny) appearance, considered to be an external variation observation, was significantly increased. Fetuses noted as having a glassy (shiny) appearance were usually the smaller fetuses within the litters and the observation was considered related to retarded fetal development within this group. No adverse effect of treatment at the high-dose level was evident from the fetal visceral evaluations. During the skeletal evaluations, the Incidence of high-dose fetuses with malformations was statistically higher than control. Skeletal malformations were seen in seven high-dose fetuses (an incidence of 6.9%) in respect to the control incidence of 0.6% (one fetus with a skeletal malformation). Two of the seven high-dose fetuses (one fetus from each of two litters) had dissimilar, relatively minor

malformations which were not considered related to treatment. Five high-dose fetuses (four fetuses from one litter and one fetus from a second litter) had one or more malformations from a syndrome of observations that involved misshapen and/or fusion defects of the exoccipital bones, fused ribs, cervical vertebral defects or involved misaligned thoracic vertebral centra. The two females whose litters contained fetuses with one or more skeletal malformations from the above stated syndrome of observations were quite stressed during the treatment period. Both females experienced weight loss during the Day 6-9 gestation interval and at day 9, were noted with marked staining of the fur in the ano-genital area and extreme soft stool; therefore, it is not clear if this syndrome of skeletal malformations as seen with increased frequency among the high-dose fetuses represents a response to treatment or is secondary to maternal toxicity encountered at this same dose level.

Test substance :

Therminol 66

Conclusion :

Therminol 66 administered by gastric intubation to pregnant CD rats during the Day 6-15 gestation interval at the 125 mg/kg/day dose level, was not considered maternally toxic, embryotoxic, fetotoxic
or teratogenic. At the 500 mg/kg/day dose level, sl1ght maternal toxicity was evident (reduced food consumption); however, no embryotoxicity, fetotoxicity or teratogenicity was indicated. At the 1500 mg/kg/day dose level, severe maternal toxicity was encountered (mortality 12.5%, reduced mean body weight data and reduced weight gain during the treatment period, reduced food consumption, and physical findings) as well as fetotoxicity (reduced fetal weights, increased incidence of fetuses with: certain ossification variations); however, no clear embryotoxicity was encountered. A statistically significant increase in the incidence of fetuses with skeletal malformations was encountered at the 1500 mg/kg/day dose level with a unique syndrome of observations seen; however, most of the affected fetuses were clustered within a single litter and it is not clear if such observations were related to a teratogenic response or more likely, to the severe maternal toxicity encountered at this dose level.

NOAELS
Maternal = 500 mg/kg-day
Developmental = 500 mg/kg-day

LOAELS
Maternal = 1500 mg/kg-day
Developmental = 1500 mg/kg-day

Reliability : (1) valid without restriction

Guideline, GLP study with full documentation.

Flag : Critical study for SIDS endpoint
13.06.2004 (23)

(1) Solutia Technical report. THERMINOL 66. 03. 10-7 (5/03).

(2) Solutia Study No. MO20020690. 1982. Vapor Pressure of MXP-2020 at Ambient Temperature.

(3) Solutia Study no. MO-77-625. 1977. Comparison of Environmental Properties of CERECLOR 42 and SANTOSOL 340.

(4) Solutia Study no. MO-95-248. 1995. Aqueous Solubility of SANTOTHERM 66.

(5) Solutia Study No. MO20020691. 1982. Sunlight photolysis screening of MXP-2020.

(6) AOP v1.90 (EPIWIN) calculation by Toxicology and Regulatory Affairs, 2004

(7) Harris, JC. Rate of Hydrolysis in Handbook of Chemical Property Estimation Methods, Lyman and Reehl eds, ACS 1990

(8) Michael Smith and Jerry March. March's Advanced Organic Chemistry, Wiley-Interscience, fifth ed 2001 chapter 6

(9) EPIWIN Calculation 2003

(10) Solutia Study no. MO20020693. 1971. Biodegradation testing of Isopropylated Biphenyl (MIBP) and HB-40.

(11) Solutia Study no. AB-79-135a. 1979. Acute toxicity of Therminol 66 to Fathead Minnows (Pimephales promelas).

(12) Solutia Study no. AB-79-135b. 1979. Acute Toxicity of Therminol 66 to Rainbow Trout (Salmo gairdneri).

(13) EPA's ECOSAR model (v. 0.99g). EPISUITE v. 3.10. US EPA (2000).

(14) Solutia Study no. MO-96-204. 1996. The Toxicity of Therminol 66 (Partially Hydrogenated Terphenyls) to Daphnia magna.

(15) Solutia Study no. AB-79-136. 1979. Acute Toxicity of Therminol 66 to Daphnia magna.

(16) Solutia study no. BN19790137 1979. Toxicity of Therminol 66 to the Freshwater Alga Selenastrum capricornutum.

(17) Solutia study no. ML19790079. 1979. Acute Oral Toxicity of HB-40 Plasticizer in Rats.

(18) Clark, CR, TC Marshall, BS Merickel, A Sanchez, DG Brownstein and CH Hobbs, 1979. Toxicological Assessment of Heat Transfer Fluids Proposed for Use in Solar Energy Applications. Toxicol. Appl. Pharmacol. 51:529-535.

(19) Solutia study no. BD19840360. 1984. Three Month Oral Toxicity Feeding Study in Rats with THERMINOL 66.

(20) Solutia Study no. DA-78-184. 1978. Salmonella Mutagenicity Assay of HB 40.

(21) Solutia Study no. SR-84-415. 1986. An Assessment of the Mutagenic Potential of THERMINOL 66 Utilizing the Acute In Vivo Rat Bone Marrow Cytogenetics Assay.

(22) Solutia Study no. ML-90-135. 1991. Two Generation Reproduction Study of THERMINOL 66 Heat Transfer Fluid in the Diet of Albino Rats.

(23) A Teratology Study in Rats with Therminol 66. Final report BioDynamics project # 84-2807 (BD-84-068) 17 February 1986